

Structure and Stereochemistry of the Alkaloid Chondrofoline

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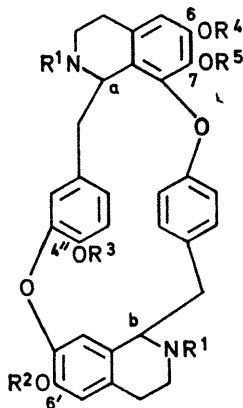
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Summary Chondrofoline has been shown to be (*S,S*)-7-*O*-methylcurine (XII) by application of n.m.r. and mass spectrometry to the alkaloid and its analogues, and to their *O*-trideuteriomethyl derivatives, for the preparation of which a simple and effective method is described.

THE recent correction¹ to the structure of chondrocurine² (I) helps elucidate the structure of the related alkaloid chondrofoline, which occurs in the leaves of *Chondrodendron platyphyllum* together with (–)-curine (II), the diastereomer of (I). Chondrofoline was isolated by King,³ and shown by degradation to have the same skeleton as curine (II). King found that chondrofoline was phenolic and had three methoxy-groups; he believed it had two secondary amino-groups, and suggested the alternative structures (III) and (IV) for it.

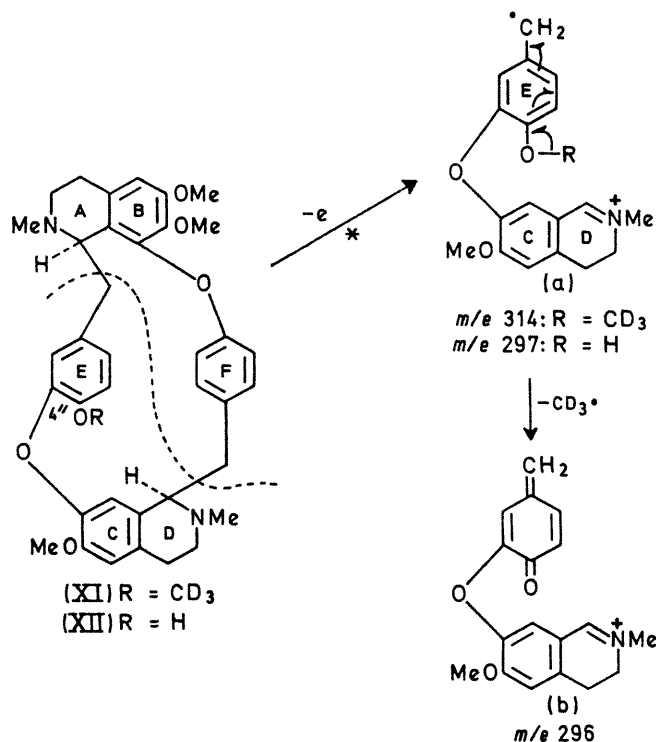
The n.m.r. spectrum⁴ of chondrofoline (CDCl₃) showed two *N*-methyl groups, and the mass spectrum confirmed it as a higher homologue of (I) and (II) with the formula C₃₇H₄₀N₂O₆. Two of the methoxy-proton resonances occurred close to τ 6.15, and the third at τ 6.26. For



- (I; R³=R⁵=H, R¹=R²=R⁴=Me; a,b=*S,R*)
 (II; R³=R⁵=H, R¹=R²=R⁴=Me, a,b=*R,R* or *S,S*)
 (III; R¹=R²=H, R³=R⁴=R⁵=Me)
 (IV; R¹=R⁴=H, R²=R³=R⁵=Me)
 (V; R¹=R²=R³=R⁴=R⁵=Me, a,b=*S,R*)
 (VI; R¹=R²=R³=R⁴=R⁵=Me; a,b=*R,R* or *S,S*)
 (VII; R¹=R²=R³=R⁴=Me, R⁵=CD₃; a,b=*S,R*)
 (VIII; R¹=R²=R³=R⁴=Me, R⁵=CD₃; a,b=*S,S*)
 (IX; R¹=R²=R⁴=Me; R³=R⁵=CD₃; a,b=*S,R*)
 (X; R¹=R²=R⁴=Me, R³=R⁵=CD₃; a,b=*R,R* or *S,S*)

† To trideuteriomethylate the phenolic groups,⁵ a diazomethane solution⁶ in light petrol was dried over KOH pellets, extracted once with an equal volume of dry dimethyl sulphoxide, which removes about 74% of the diazomethane, and then added to a solution of the alkaloid in dry dimethyl sulphoxide containing a few drops of heavy water. If necessary, the addition is repeated daily.

alkaloids in this series, the lower values correspond to methoxy-groups at the less crowded 6 positions of the isoquinoline residues, and the higher one to a 7-methoxy-group or one attached to the 4'' position of a benzyl group.⁴



The latter positions were readily distinguished in model compounds by measuring the spectra again, in C₆D₆, after first trideuteriomethylating† any free hydroxy-groups to eliminate effects of internal hydrogen-bonding. The results for (I) and (II), their 4''-*O*-methyl derivatives (the naturally-occurring alkaloids hayatidine⁷ and 4''-*O*-methylcurine⁸), their *OO*-dimethyl derivatives (V) and (VI), and chondrofoline are shown in the Table. The two diastereomeric series are clearly differentiated by the pattern of the OMe and particularly of the NMe proton peaks; in each case, the 4''-*O*-methyl protons resonate at highest field, while the 7-*O*-methyl is lowest, as can be expected for a

methoxy-group with two *ortho*-ether substituents.⁹ *O*-Tri-deuteriomethylchondrofoline (XI) evidently belongs to the curine series, with methoxy-groups at the 6, 6', and 7

4''-methoxy-group;¹⁰ however, the corresponding ion from *O*-trideuteriomethylchondrofoline (XI) specifically loses CD₃ to give a strong ion (b) at *m/e* 296.¹⁰ Furthermore,

Methoxy and N-methyl proton resonances of chondrocurine and curine derivatives (τ)

	7	OMe 6 and 6'	4''	NMe 2 and 2'
<i>OO</i> -Dimethylchondrocurine (V)	6·37	6·53, 6·53	6·57	7·72, 7·97
<i>O</i> -Trideuteriomethylhayatidine (VII)	—	6·55, 6·58	6·60	7·75, 7·95
Bistrideuteriomethylchondrocurine (IX)	—	6·54, 6·54	—	7·73, 7·94
<i>OO</i> -Dimethylcurine (VI)	6·38	6·48, 6·58	6·70	7·72, 7·76
<i>O</i> -Trideuteriomethyl-4''- <i>O</i> -methylcurine (VIII)	—	6·49, 6·59	6·72	7·72, 7·75
Bistrideuteriomethylcurine (X)	—	6·48, 6·58	—	7·73, 7·76
<i>O</i> -Trideuteriomethylchondrofoline (XI)	6·37	6·49, 6·60	—	7·73, 7·76

positions, and chondrofoline is thus represented by (XII); its o.r.d. curve shows it to be related to (–)-curine (S,S).

The mass spectra confirm the structures (XI) and (XII): in particular, the ion (a; R=H) formed from rings c,d, and e of chondrofoline (XII) by the cleavages shown has little tendency to lose CH₃· in contrast to analogues with a

both (XI) and (XII) give a prominent ion at *m/e* 204, characteristic of alkaloids in this series with methoxy-groups at C-6 and C-7 of ring B.¹⁰

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